Oxalic Acid

CAS #144-62-7
Swiss CD-1 mice, at 0.0, 0.05, 0.1, 0.2%, drinking water
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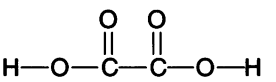

Oxalic acid (OA), a metabolite of ethylene glycol, was selected for testing in the RACB protocol based on the biological activity of the parent compound (Morrissey et al., Fundam Appl Toxicol 13:747–777 [1989]). It was part of a series of glycol ethers, congeners, and metabolites evaluated for structure–activity correlations using this design. Data collected on body weights, clinical signs, and food and water consumption during the dose-range-finding segment (Task 1) were used to set concentrations for the main study (Task 2) at 0.05, 0.10, and 0.2% OA in drinking water. These concentrations reduced water consumption in the middle and high dose groups by less than or equal to 25%, and yielded calculated consumption estimates of approximately 89, 162, and 275 mg OA/kg/day. There were no adverse clinical signs.

One female died in both the low and middle dose groups. At 0.2% OA, the number of litters per pair was reduced by 5% and the pup weight adjusted for litter size was reduced by approximately 4%; sire and dam weights were not affected during Task 2. For the last litter born in Task 2, body weights and pup number were recorded for the controls and 0.1 and 0.2% OA groups; there were no treatment-related changes in pup survival or weight gain to postnatal day 14.

Based on the fact that a modest degree of effect seen at the top dose group in Task 2 was identified only after summing all the Task 2 litter data, it was predicted that the single litter produced in Task 3 would be insufficient to help determine the affected sex. Thus, the last litter from the control and high dose animals were reared for testing in Task 4.

After the Task 4 mice were weaned, ten F_0 mice from the control and 0.2% groups were killed and necropsied. No changes were seen in body or organ weights from females. For males, the only significant effect was a 19% decrease in prostate weight at 0.2% OA. Total calcium levels in blood were measured for 10 mice of each sex in the control and 0.2% OA groups; the control level of 9.4 mg/dl was unchanged due to treatment.

In the Task 4 1-week mating trial, there was a 20% reduction in the number of live pups per litter delivered by the 0.2% OA group. No other differences were observed. After 7 days of vaginal lavage, the F_1 mice were killed and necropsied. While terminal body weight was unchanged in either sex, female kidney weight (adjusted for body weight) was increased by 10% in the OA-treated females. There were no other changes in organ weights. The percent of abnormal sperm forms increased from 2.2% in controls to 4.0% in the 0.2% OA group. Serum calcium levels in either sex were unchanged from control levels of 7.9 mg/dl.

In summary, in the F_0 mice, oxalic acid at these levels reduced water consumption, and reduced the number of litters per pair, adjusted pup weight, and prostate weight in the absence of detected somatic organ changes. In F_1 mice, an increase in kidney weight occurred concomitant with a reduction in the number of live pups per litter, and increased abnormal sperm forms. If the kidney weight effect is the result of reduced water consumption, then it can be concluded that oxalic acid is a reproductive toxicant in Swiss CD-1 mice at concentrations that reduce parental water consumption, but that cause few other somatic effects.

Summary: NTP Reproductive Assessment by Continuous Breeding Study.

NTIS#: **86167053/AS**
Chemical: **Oxalic Acid**
CAS#: **144-62-7**
Mode of exposure: **Drinking water**
Species/strain: **Swiss CD-1 mice**

F_0 generation — Dose concentration →	0.05%	0.10%	0.20%
General toxicity	Male, female	Male, female	Male, female
Body weight	—, —	—, —	—, —
Kidney weight[a]	•	•	—, —
Liver weight[a]	•	•	—, —
Mortality	—	—	—, —
Feed consumption	•, •	•, •	•, •
Water consumption	—, —	↓, ↓	↓, ↓
Clinical signs	—, —	—, —	—, —
Reproductive toxicity			
x̄ litters/pair	—	—	↓
# live pups/litter; pup wt./litter	—, —	—, —	—, ↓
Cumulative days to litter	—	—	—
Absolute testis, epididymis weight[a]	•, •	•, •	—, —
Sex accessory gland weight[a] (prostate, seminal vesicle)	•, •	•, •	↓, —
Epidid. sperm parameters (#, motility, morphology)	•, •, •	•, •, •	—, —, —
Estrous cycle length	•	•	—

Determination of affected sex (crossover)	Male	Female	Both
Dose level	•	•	•

F_1 generation — Dose concentration →	0.05%	0.10%	0.20%
General toxicity	Male, female	Male, female	Male, female
Pup growth to weaning	•	•	•
Mortality	•, •	•, •	—, —
Adult body weight	•, •	•, •	—, —
Kidney weight[a]	•	•	—, ↑
Liver weight[a]	•	•	—, —
Feed consumption	•, •	•, •	•, •
Water consumption	•, •	•, •	—, —
Clinical signs	•, •	•, •	—, —
Reproductive toxicity			
Fertility index	•	•	—
# live pups/litter; pup wt./litter	•, •	•, •	↓, —
Absolute testis, epididymis weight[a]	•, •	•, •	—, —
Sex accessory gland weight[a] (prostate, seminal vesicle)	•, •	•, •	—, —
Epidid. sperm parameters (#, motility, morphology)	•, •, •	•, •, •	—, —, ↑
Estrous cycle length	•	•	—

Summary information	
Affected sex?	Unclear
Study confounders:	None
NOAEL reproductive toxicity:	Not determined
NOAEL general toxicity:	Not determined
F_1 more sensitive than F_0?	Unclear
Postnatal toxicity:	No

Legend: —, no change; •, no observation; ↑ or ↓, statistically significant change ($p<0.05$); —, —, no change in males or females. [a]Adjusted for body weight.